

REMARKS

Informalities

Claim 4 has been amended at the Applicant's initiative to remove duplicate wording.

Restriction Requirement under 35 U.S.C. § 121

An election requirement was made to pending claims 1-19. The claims were placed into eight groups:

Group I (claims 1-4, 7 and 11) drawn to a method of treating or preventing dementia comprising administering an effective amount of MCT or a prodrug thereof;

Group II (claims 5-6, 8-9 and 13 (in part)) drawn to a method of treating or preventing dementia comprising administering an effective amount of L-carnitine;

Group III (claim 10) drawn to a method of treating or preventing dementia comprising administering an effective amount of free medium chain fatty acid;

Group IV (claim 12) drawn to a method of treating or preventing dementia comprising administering an effective amount of a therapeutic agent which induces utilization of fatty acid and the development of ketones;

Group V (Claims 13 (in part) and 14-15) drawn to a method of treating or preventing dementia comprising administering an effective amount of L-carnitine and a therapeutic agent;

Group VI (Claims 16-18) drawn to a composition comprising an MCT or prodrug thereof;

Group VII (Claim 17) drawn to a composition comprising free medium chain fatty acid; and

Group VIII (Claim 19) drawn to a composition comprising a therapeutic agent which induces utilization of fatty acid and development of ketones.

In a telephone conversation with the Examiner on June 16, 2000, Applicant made a provisional election to prosecute the invention of Group I, claims 1-4, 7 and 11. Applicant hereby affirms the election of claims 1-4, 7 and 11 without traverse.

The Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected Claims 1-4, 7 and 11 under 35 U.S.C. § 103(a) as being unpatentable over Mak, et al., CABA database AN 1999:136034 (1999), and Veech

(U.S. Patent No. 6,316,038). The Examiner bears the burden of establishing a *prima facie* case of obviousness (Section 103). In determining obviousness, one must focus on Applicant's invention as a whole. *Symbol Technologies Inc. v. Opticon Inc.*, 19 U.S.P.Q.2d 1241, 1246 (Fed. Cir. 1991). The primary inquiry is:

whether the prior art would have suggested to one of ordinary skill in the art that this process should be carried out and would have had a reasonable likelihood of success Both the suggestion and the expectation of success must be found in the prior art, not in the applicant's disclosure.

In re Dow Chemical, 5 U.S.P.Q.2d 1529, 1531 (Fed. Cir. 1988).

The Examiner asserts that Veech teaches a method for treating Alzheimer's disease and its symptoms and manifestations, including dementia employing a ketogenic diet of medium chain triglycerides, and also teaches an example of a ketogenic diet wherein at each of the three meals the patient consumes 48-50 grams of fat. The Examiner further asserts that Veech teaches that increase of ketone bodies is effective in the treatment of Alzheimer's disease, and the oral and parenteral administration of triglycerides can increase blood ketones. Finally, the Examiner asserts that Mak, et al. teaches that ketogenic diets are known to improve cognitive functioning.

The Examiner reasons that it would have been obvious to one of ordinary skill in the art at the time the invention was made to employ medium chain triglycerides in a method of treating Alzheimer's disease and dementia associated therewith, because medium chain triglycerides are known to increase the level of ketone bodies in the blood and the increase of ketone bodies in the blood is known to be useful in treating Alzheimer's disease.

Applicant respectfully traverses the rejection. The present claims are directed toward a method of treating or preventing dementia of Alzheimer's type, or other loss of cognitive function caused by reduced neuronal metabolism, comprising administering an effective amount of medium chain triglycerides or a medium chain triglyceride prodrug thereof to a patient in need thereof.

In contrast, the cited passages in the prior art references refer to ketogenic diets. Veech, at column 10, lines 56-68 describes the "classic" ketogenic diet, while Mak, et al. describes a medium chain triglyceride (MCT) oil ketogenic diet. Submitted herewith is a copy of the entire Mak, et al. reference which more clearly explains the information in

the abstract provided by the Examiner: Mak, et al. Acta Paediatr. Sin. (1999) 40:97-100. Mak, et al. and Veech explain that the classic ketogenic diet used long-chain fatty acids which were unpalatable. The introduction of the medium chain triglyceride oil diet increased compliance with the diet due to greater palatability.

As pointed out by Mak, et al., and Veech, the ketogenic diet is a high fat, low carbohydrate, low protein, regimen. Veech explains, at column 11, lines 47-54 that carbohydrate ingestion must be avoided in a ketogenic diet due to the metabolic consequences associated with carbohydrate ingestion, namely, an unwanted drop in blood ketones and the esterification of lipids to triglycerides in the liver.

Applicant notes that the Veech patent contains a factual error. Veech provides that heavy cream used in an example of a ketogenic diet at col. 10., lines 67-68 is “comprised mainly as medium chain triglycerides.” The United States Department of Agriculture Nutrient Database provides nutritional data for heavy cream (information enclosed, and available at <http://www.nal.usda.gov/fnic/foodcomp/>). The USDA data provides that 100 g of fluid heavy whipping cream contains about 33 grams of total fat (saturated and unsaturated) of which only 9% (3 grams) are MCTs. (MCTs are defined as triglycerides with fatty acid moiety chain lengths between 6-12 carbons, relevant cells of the table are shaded). Thus, it can not be said that heavy cream is “comprised mainly as medium chain triglycerides.” The diet provided by Veech is a not an MCT ketogenic diet as provided in Mak, et al, but is rather a classic ketogenic diet utilizing long-chain fatty acids.

Both Mak, et al, and Veech provide descriptions of ketogenic diets in which fat is high and carbohydrates are limited. In summary, although Mak, et al., and Veech provide that the intake of high amounts of fat, whether long-chain or medium-chain triglycerides, can increase blood ketone levels, this result occurs only in the context of a highly-regimented diet in which carbohydrate levels are limited. Veech explicitly states at col. 9, lines 62-65, that “Either oral or parenteral administration of free fatty acids or triglycerides can increase blood ketones, *provided carbohydrate and insulin are low to prevent re-esterification in adipose tissue.*” (emphasis added). Similarly, Mak, et al., at p. 98, column 2, teaches that “protein was given as 1.5-2 gm/kg/day, carbohydrates were given in terms of less than 19% of the total calorie requirement. Total calories supplied

from protein and carbohydrates should not have exceeded 29% of the total daily calorie requirement.”

In contrast, the present invention provides for and claims the administration of medium chain triglycerides outside of the context of the ketogenic diet. The use of the transition “comprising” indicates that other components, including carbohydrates, may be administered as well. The EXAMPLES section of the application provides exemplary formulations which include carbohydrates. Example 2B, for instance, provides a formulation for a powdered beverage utilizing maltodextrin and sucrose. In providing that triglycerides can only be administered in a diet of low protein and carbohydrate, the Mak, et al., and Veech references teach away from the present invention, which provides for the use of MCTs when not part of the ketogenic diet.

The Examiner asserts that Mak, et al., teaches that ketogenic diets are known to improve cognitive functioning. More precisely, Mak, et al. provides that in patients that had a significant decrease in seizure frequency (>75%) after following a ketogenic diet also had some degree of improvement in cognitive function. Thus, the improvement in cognitive function is associated with reduction in seizures.

As explained above, the present invention providing for administration of MCTs is distinct from the ketogenic diet. Moreover, the patients in the Mak, et al., article were children, as are the subjects in most ketogenic diet studies. In contrast, most Alzheimer’s patients are elderly adults. Applicant submits that one skilled in the art would not be motivated to look to treatments for refractive epilepsy in children for guidance in the treatment of Alzheimer’s disease in adults, particularly elderly adults. Mak, et al., neither teaches nor suggests that the cognitive improvement associated with reduction in seizure frequency may be applied to other conditions which have reduced cognitive function as a symptom. Additionally, Mak, et al. addresses refractive epilepsy, which is a subclass of the disease where the patient does not respond to conventional drug therapy.

Neither Mak, et al., nor Veech teach or suggest that MCT’s alone, outside the context of the ketogenic diet may be used to treat Alzheimer’s disease. On the contrary, the references explicitly teach that carbohydrate intake must be limited. At most, the combination of Mak, et al., and Veech make it “obvious to try” to use an MCT ketogenic diet in the treatment of Alzheimer’s disease. It is well-settled that “obvious to try” is an

improper consideration in an obviousness rejection. *See Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 231 U.S.P.Q. 81, 91 (Fed. Cir. 1986).

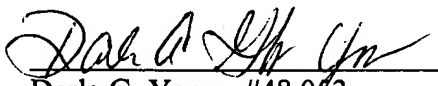
Applicant notes that the ketogenic diet has been known for decades, and the MCT ketogenic diet has been known since at least the '70s for the treatment of epilepsy. Also, it has been known for many years that seizure control may be associated with improved cognitive function, and that cognitive impairment is associated with Alzheimer's disease. Applicant is unaware of any prior art teaching or suggesting that MCT therapy be used to treat Alzheimer's disease or other cognitive disorders, indicating that it was not obvious to persons skilled in the art to do so. That is, the skilled person was not motivated to apply treatments for epilepsy due to the fact that the underlying cause of epilepsy has not been shown to be similar to that of Alzheimer's disease. Reconsideration is respectfully requested.

Closing Remarks

Applicant believes that the pending claims are in condition for allowance. If it would be helpful to obtain favorable consideration of this case, the Examiner is encouraged to call and discuss this case with the undersigned.

This constitutes a request for any needed extension of time and an authorization to charge all fees therefore to deposit account No. 19-5117 if not otherwise specifically requested. The undersigned hereby authorizes the charging of any fees created by the filing of this document or any deficiency of fees submitted herewith to deposit account No. 19-5117.

Respectfully submitted,


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Enclosures: Mak, et al, *Acta Paediatr. Sin.* (1999) 40:97-100.
Table 1. Cream, fluid, heavy whipping.

Marked up version showing changes to claims under 37 C.F.R. § 1.121(c)(ii)

4. The method Claim 1, wherein said medium chain triglycerides are administered ~~medium chain triglycerides are administered~~ at a dose of about 0.5 g/kg/day to about 10 g/kg/day.

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